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INTRA-MYOCARDIAL DELIVERY OF INDUCED PLURIPOTENT STEM CELLS ENHANCES CARDIAC REPAIRS AND AMELIORATES LEFT VENTRICULAR DYSFUNCTION FOLLOWING MYOCARDIAL INFARCTION IN RATS

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Objectives Aging and aging-related disorders of mesemchymal stem cells transplantation impair the efficiency and function of differentiation toward cardiomyocytes after myocardial infarction. Induced pluripotent stem cells (iPSCs) may provide an alternative source of functional MSCs for cardiomyocytes repair after MI. This study aimed to evaluate the effect of intra-myocardial iPSC-MSCs transplantation on myocardial function and investigate their biological function for the treatment of acute myocardial infarction.

Methods An MI model in rat was created by ligation of left main coronary artery. Female Sprague-Dawley rats were randomed into three groups: AMI (group control), MSCs transplantation (group M), iPSC-MSCs transplantation (group iM). MSCs and iPSC-MSCs were injected into LV free wall in the region bordering an infarct in recipient rats following AMI. 3 and 7 days after MI, the EGFP donor cells were traced in MSCs recipient rats by fluorescence microscopy. The inflammatory cytokines' mRNA expression were determined by means of RT-PCR.TUNEL and H&E staining were used to assess apoptosis and pathological changes, respectively. LV function was detected using echocardiography.

Results The benefits of iPSC-MSCs on acute myocardial infarction were superior to those of adult bone marrow MSCs. IPSC-MSCs therapy attenuated MI-induced inflammatory factors, apoptosis and decreased pathological damaged compared with BM-MSCs, especially at 7 day. MI-dilated LV with impaired function significantly reduced fractional shortening, cardiomyocytes peak shortening and relengthening. All of these parameters were improved by iPSC-MSCs therapy which were superior to BM-MSCs and control group at both of 3 and 7 days.

Conclusions Intra-myocardial delivery of induced pluripotent stem cells could selectedly migrate to peri-infarct area, attenuated MI-induced apoptosis and restored LV function. Taken together, transplantation of iPSC-MSCs represent a new treatment strategy to improve cardiac function after MI superior to bone marrow MSCs with higher security and efficiency.